JOURNAL OF NUCLEAR MEDICINE 7:807-816, 1966

Elimination of Liver Interference from the Selenomethionine Pancreas Scan[1]

Ervin Kaplan, M.D., Moshe Ben-Porath, B.S., Sidney Fink, M.D., Glenn D. Clayton, B.S. and Burton Jacobson, M.D.

Hines, Illinois

Diagnosis of pancreatic disease by visualization of this organ has presented many technical difficulties. The synthesis of ^{75}Se selenomethionine has been a major step in making possible the display of this organ by scanning techniques (1, 2, 3, 4). The simultaneous localization of selenomethionine in the liver has been a serious limiting factor in definition and delineation because the proximity of the two organs may result in the liver anatomically overlying the pancreas. Numerous attempts have been made to partially resolve this interference. These methods include shielding the liver with lead (5); increasing the pancreatic uptake with pancreozymin (6) and amino acids (7); retaining the pancreatic secretions by constricting the sphincter of Oddi with morphine (8); and decreasing the volume of secretion without altering uptake through use of propantheline bromide (Probanthine) (7).

The capacity of the liver to concentrate gamma-emitting isotopes not concentrated by the pancreas has been used to separately scan the liver. The limits of this organ are then determined by superimposing the liver scan upon the combined liver and pancreas scan obtained by conventional ^{75}Se selenomethionine scanning (9). While the limits of the liver are defined by this method, the limits of the pancreas are not.

The use of two channel pulse height analyzer systems has been proposed. Initial studies of ^{65}Zn and ^{131}I Rose Bengal were not successful (10). Computer derived iso-response figures using a liver-seeking isotope and ^{75}Se selenomethionine has been reported in a model system using a two-channel device (11). A similar system has been reported by Spencer (12), but has not to our knowledge been applied to the pancreatic scanning problem.

[1]From the Radioisotope and Medical Services, Veterans Administration Hospital, Hines, Illinois, and the Departments of Medicine, University of Illinois College of Medicine and Loyola University, Stritch School of Medicine.

Adaptation of conventional scanning equipment and a commercially available dual channel pulse height analyzer, countrate system has been made for the purpose of eliminating the liver image from the pancreatic scan. This system is described below, as well as the results obtained in scanning a model system and the pancreas in human subjects (13).

METHOD AND EQUIPMENT

The patient is injected intravenously with both labeled selenomethionine and colloidal ^{198}Au as described below. The selenomethionine is concentrated in the liver and pancreas, the gold in only the liver. Predicated upon this differential distribution, the three or five-inch NaI(Tl) detector of a commercial scintiscanner[1] equipped with a five-inch focal length focusing collimator is placed over the right lobe of the liver remote from the pancreas. As described in the block diagram, Figure 1, the output of the detector is coupled to a dual channel pulse height analyzer, countrate meter system. One channel detects the 411 kev ^{198}Au photopeak, the other simultaneously detects the 280 kev ^{75}Se photopeak, each through a 100 kev window. The output of the two analyzers is coupled to two countrate meters. The ^{198}Au and the ^{75}Se counts are separately observed. The countrates are balanced to be equal. The ^{198}Au output is placed in a subtract mode, and the two outputs are coupled through a DC to frequency converter, Figure 2, to the input of the scanner.

The patients were prepared by one of the following methods:

METHOD ONE

The patient is prepared by fasting overnight. Breakfast consists of 300 grams of gelatin dessert containing 4.5 grams of protein, which is fed because of its relatively low methionine content. In the presence of abundant other amino acids, selenomethionine concentration in the pancreas may be enhanced. Thirty minutes following this meal, the patient is administered 100 μC of ^{198}Au colloid by intravenous injection. Seventy-five minutes after breakfast, the patient received 1/8 to 1/4 grains of morphine sulfate, the dose depending upon the patient's weight and tolerance, to assure constriction of the Spincter of Oddi (14). Fifteen mg of propantheline bromide (Probanthine) are administered at this time to decrease the fluid volume of the pancreatic secretion (15). The two agents used simultaneously should prevent phenomena related to increased intraluminal pressure in the pancreatic ducts (16), without altering selenomethionine accumulation.

METHOD TWO

The patient received a regular breakfast followed in 30 minutes by 100 μC of ^{198}Au colloid by intravenous injection.

Common to the two methods, 90 minutes to 120 minutes after breakfast, the patient is placed supine with the detector over the right lobe of the liver. Two hundred and fifty microcuries of ^{75}Se selenomethionine are administered intra-

[1]Picker Magnascanner III or IV

venously. The countrate for ^{198}Au and ^{75}Se are observed simultaneously. Within 10 to 15 minutes the ^{75}Se count stabalizes. The amplitude of deflection of the two meters is equated by a balancing circuit or by window width adjustment. The ^{198}Au is subtracted. The patient is scanned at a speed of 30 cm per minute at 4 mm line interval. The scan is completed in 30 minutes. The equality of the ^{198}Au counts and the ^{75}Se counts are rechecked over the right lobe of the liver, adjusted if necessary, and the scan may be repeated.

Method two appears equally effective when compared with method one and is now used exclusively.

The system was evaluated by several means. The initial evaluation was de-

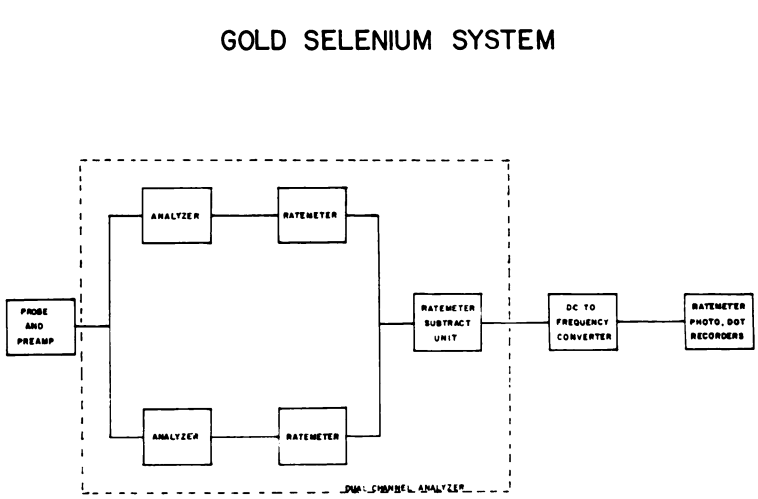

Fig. 1. Block diagram of the circuitry employed in dual channel subtract scanning system.

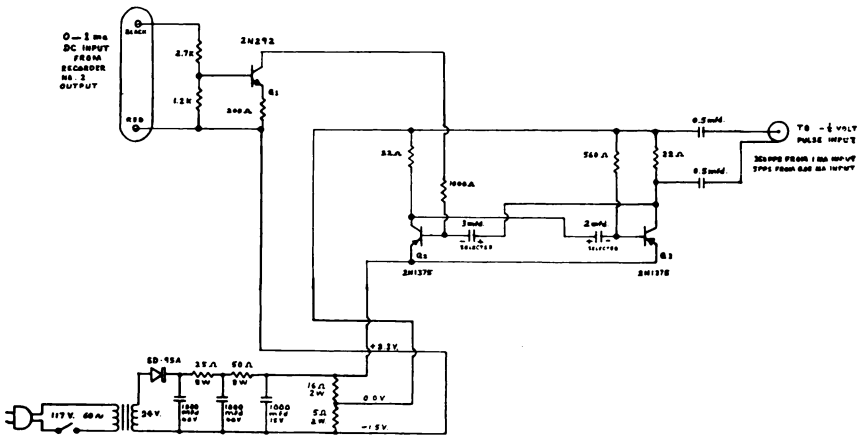

Fig. 2. Circuit details of the DC to frequency converter employed in coupling the negative and positive outputs of the dual channel system.

termined upon a model system. The model pancreas was a plastic container filled with 75 microcuries of ^{75}Se solution, while the liver was represented by a Marinelli-type plastic container with a hollow center. This container was filled with a solution of 90 microcuries of ^{198}Au and 90 microcuries of ^{75}Se.

The system was subsequently tested upon 25 male subjects subjected to the regimen and dosage above described. The pancreas was scanned serially after administration of the labeled selenomethionine for periods up to 30 hours. Fourteen patients have been subjected to three or more serial scans. The anatomical configuration has been noted in the scans studied. Comparison is made with conventional pancreatic scanning.

Six patients with known pancreatic pathology have been scanned to this time as a prelude to more intensive evaluation of pancreatic disease by scanning.

RESULTS

The results of scanning the model system described above may be visualized in Figure three. The ^{75}Se within the inner plastic bottle may be visualized clearly when the ^{198}Au and ^{75}Se in the outer container are eliminated by subtracting gold from selenium.

In the 25 patients scanned, the pancreas was consistently visualized with

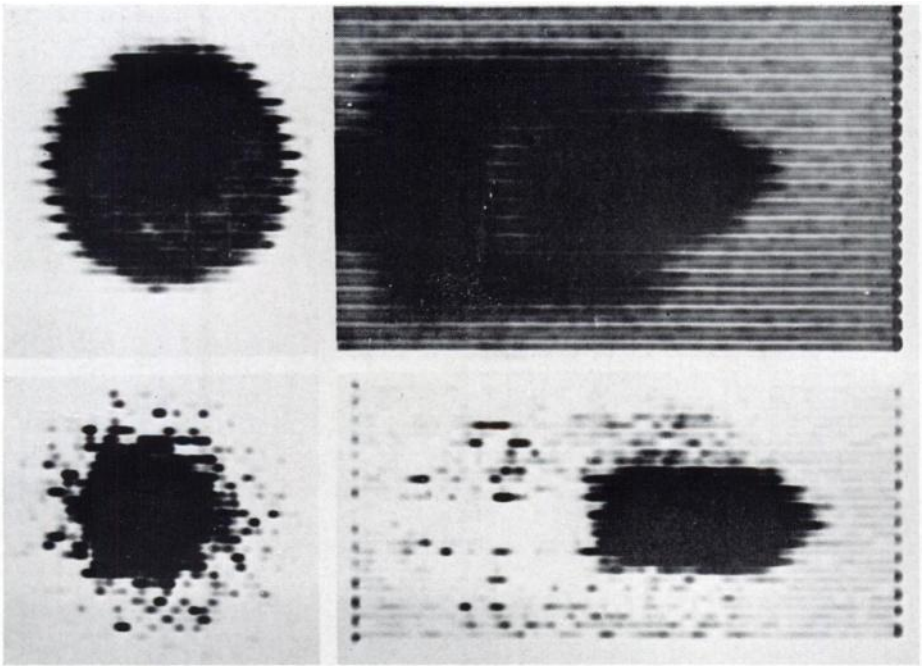

Fig. 3. (a) End on scan of ^{75}Se activity in two concentric containers, visualizing ^{75}Se gamma photo peak. (b) Scan of ^{75}Se activity in two concentric containers, visualizing ^{75}Se gamma photo peak. Lateral view. (c) End on scan of ^{75}Se activity in two concentric containers, outer container neutralized by subtraction of ^{198}Au activity from ^{75}Se activity. (d) Scan of ^{75}Se activity in two concentric containers, outer container neutralized by subtraction of ^{198}Au activity from ^{75}Se activity. Lateral view.

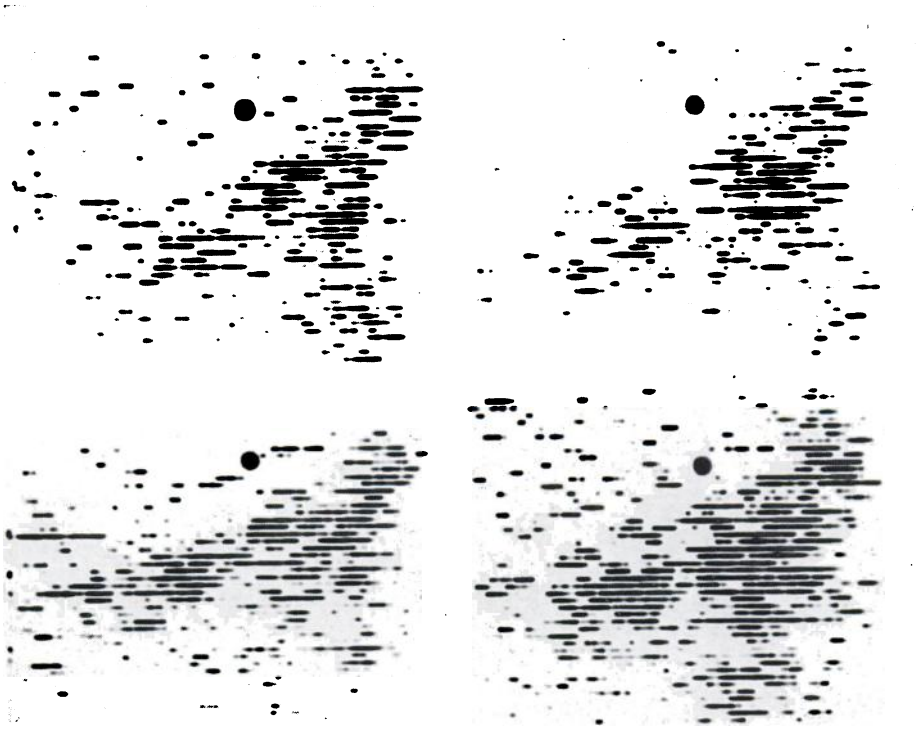

Fig. 4. Pancreatic scan by gold subtract method, showing progressive accumulation of ^{75}Se activity at (a) 30 minutes (b) 2 hours 30 minutes (c) 4 hours 30 minutes, and (d) 6 hours 40 minutes following injection of ^{75}Se seleonomethionine. The subject was a 49-year-old male with normal pancreatic function.

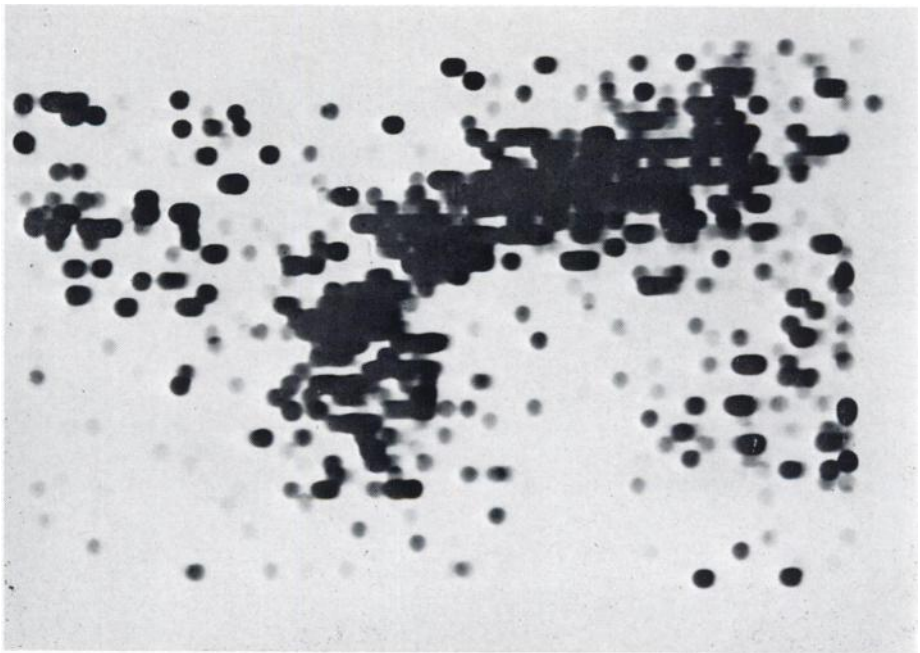

Fig. 5. Selenomethionine pancreas photoscan by gold subtract method from a 75-year-old male subject showing pistol-shape configuration.

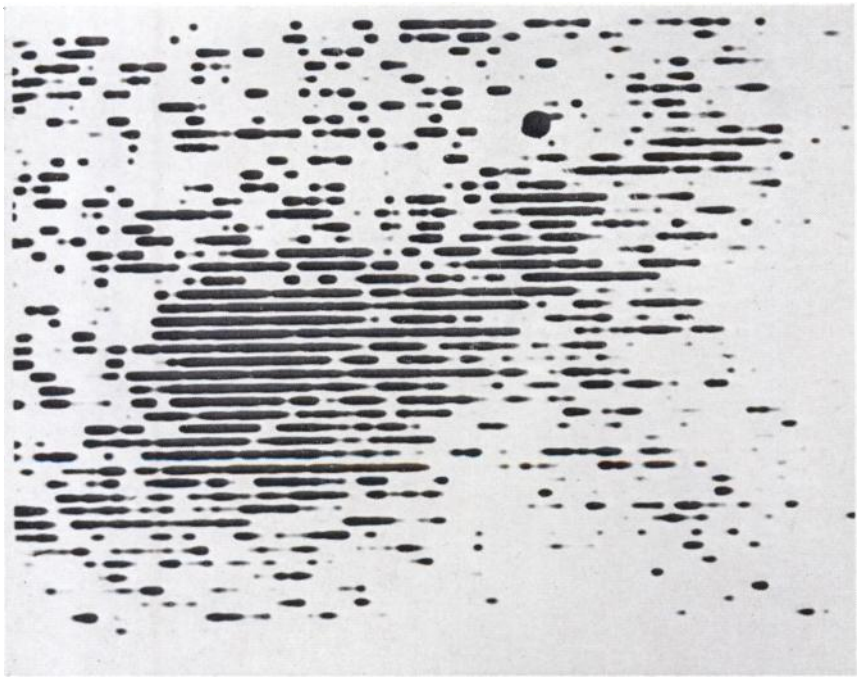

Fig. 6. Selenomethionine pancreas photoscan by gold subtract method from a 40-year-old male subject showing large head and small tail.

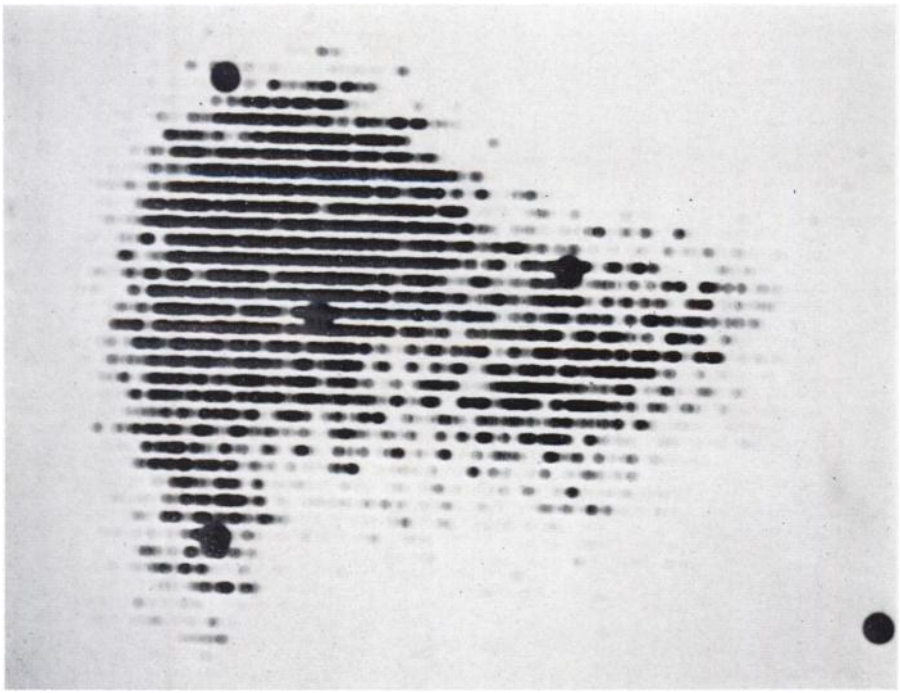

Fig. 7a. A photoscan of the distribution of ^{198}Au in the liver of a 37-year-old male subject.

the exception of three patients early in the series, while technical improvement in the circuitry was still being made.

Serial scanning indicated continuous accumulation of ^{75}Se in the pancreas for periods up to seven hours following intravenous administration of labeled selenomethionine. This criteria for accumulation was successively denser pancreatic images with the maintenance of constant scanner control settings and patient-detector geometry (See Figure 4). Such accumulation was decreased by a regular lunch, but was not effected by substituting a glass of orange juice for lunch.

The principal anatomical variations in the normal pancreas encountered in this study are exemplified by the pistol-shaped pancreas, (Figure 5); the pancreas with a large head and small tail, (Figure 6), and the most common variant encountered in this study in which the tail is more massive than the head and a marked attenuation is observed where the pancreas crosses the vertebrae, (Figure 7c). This latter figure also compares the ^{198}Au liver scan (7a), the ^{75}Se scan (7b) and the gold subtract scan which eliminates the liver (7c).

Insufficient cases of carcinoma of the pancreas and chronic pancreatitis have been completed to make any significant evaluation of this technique in pancreatic pathology. Two illustrative scans are included to indicate our preliminary findings in pancreatic disease. Figure 8 shows the pancreatic scan in carcinoma of the pancreas. The day following the scan, laparotomy demonstrated that this 59-year-old white male with obstructive jaundice had virtual destruction of the head of the pancreas and a portion of the tail by carcinoma. Figure 9 indi-

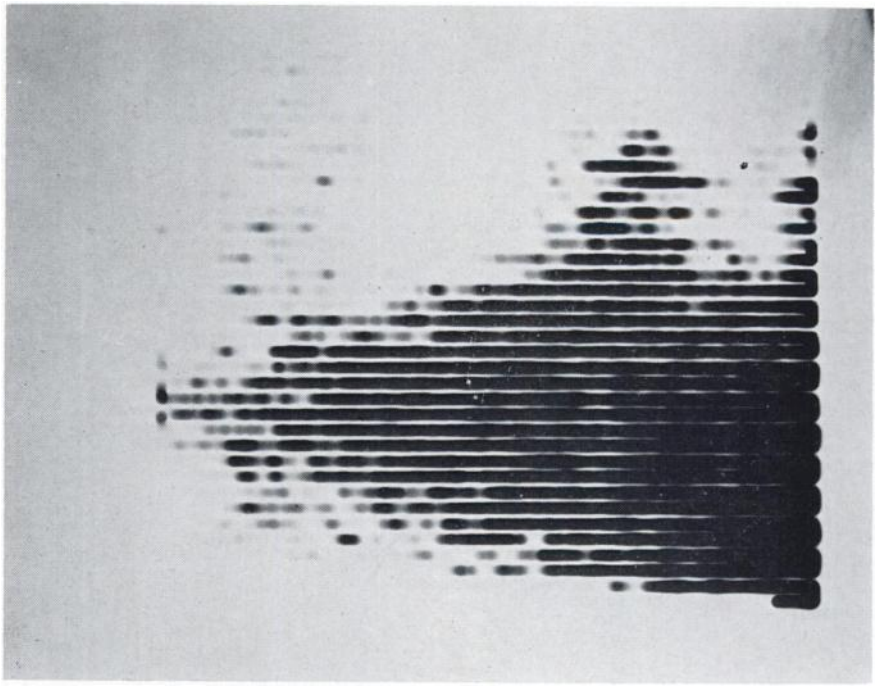

Fig. 7b. A photoscan showing distribution of ^{75}Se in the liver and pancreas of the subject in (a). Note the overlap of the two organs.

cates a scan obtained in a 42-year-old male with a history of chronic pancreatitis. The pancreas was visualized, but was markedly shrunken in size. Decreased size was not necessarily an observed characteristic in other patients with this diagnosis.

DISCUSSION

The routine visualization of the normal pancreas without interference from the liver may now be accomplished using conventional three-inch and five-inch detectors and scanning systems with the subtract system described. The patient may be adequately prepared by eating a regular breakfast. The continuing accumulation of ^{75}Se in the pancreas would suggest that the most appropriate time for the scan would be four hours following breakfast and two hours following the injection of labeled selenomethionine. The mechanism of continued accumulation should be further investigated, as free selenomethionine has been reported to disappear from the circulation in approximately 30 minutes and reappear as protein-bound ^{75}Se activity (17). The mechanism of accumulation from the protein-bound moiety suggests, but certainly does not verify, incorporation of more complex molecules than amino acids by the pancreas.

Use of the subtract technique for scanning can be accomplished with smaller dosage of ^{75}Se and ^{198}Au than was used in the current study. It is suggested that evaluation of pancreatic disease may be enhanced by this technique. Its application in scanning other organs is indicated.

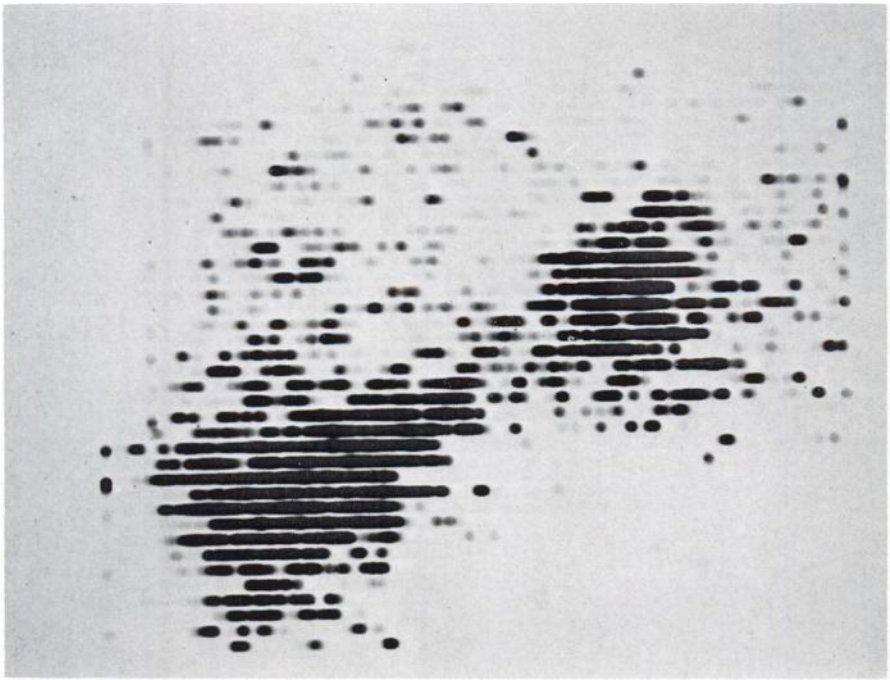

Fig. 7c. A photoscan of the ^{75}Se selenomethionine in the pancreas of the subject in (a) obtained using the gold subtract technique. Note the attenuation of the pancreas as it overlies the vertebrae.

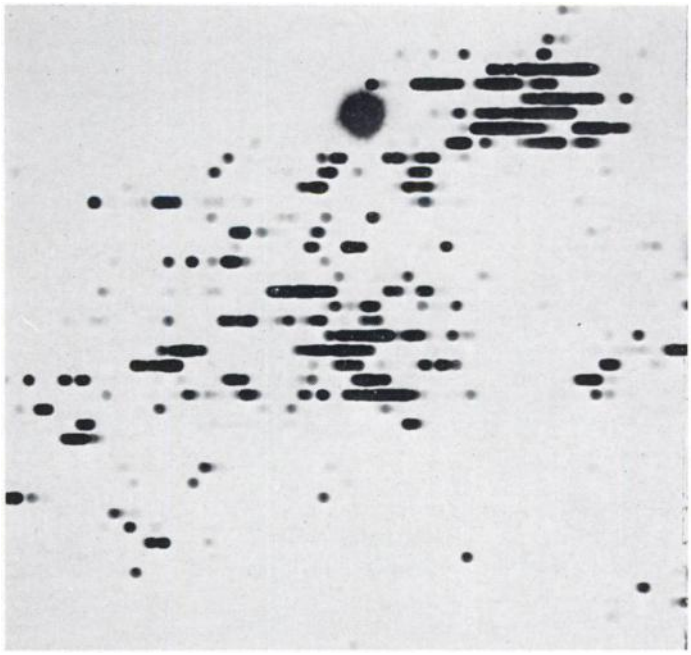

Fig. 8. A selenomethionine gold subtract photoscan of a 59-year-old male patient with severe obstructive jaundice. At surgery on the day following this scan, the patient was found to have a carcinoma of the pancreas with massive replacement of the head of the pancreas and a portion of the tail.

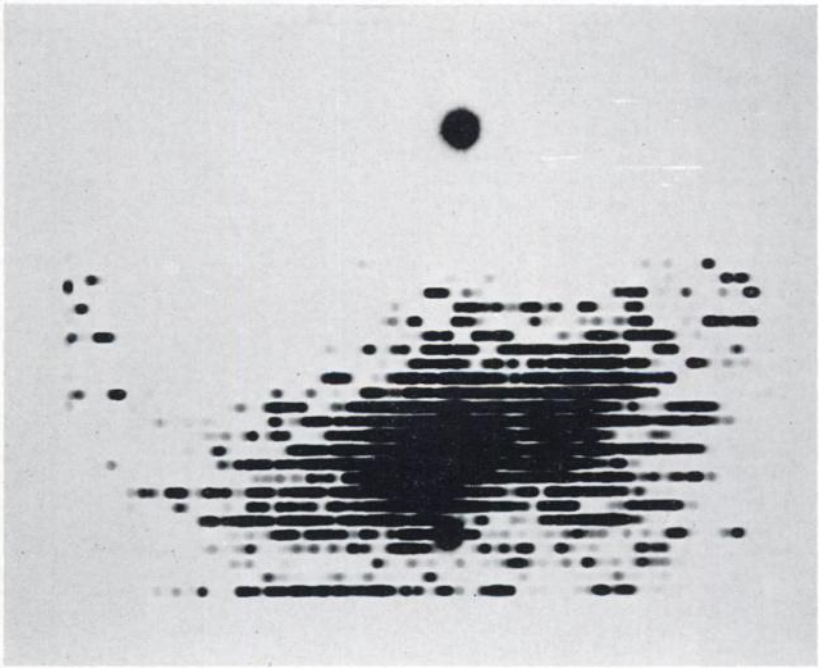

Fig. 9. A selenomethionine photoscan using gold subtract method of the pancreas of a 42-year-old male patient with chronic pancreatitis. This pancreas was shrunken in size; its length was 10 cm as compared to 15 to 20 cm length seen in normal subjects.

SUMMARY

A method of scanning the pancreas is described, in which the liver image is eliminated by the subtraction of the radio gold photopeak from that of selenium-75. The electronic system is pictured in block and detailed circuit diagram. The system has been useful in consistently producing a pancreatic image.

ACKNOWLEDGMENT

We wish to acknowledge the cooperation in this study of Picker Nuclear Division of Picker X-Ray Corporation, and Dr. Paul Numerof of E. R. Squibb and Sons.

REFERENCES

1. KAPLAN, E., CLAYTON, G., FINK, S., JACOBSON, B. AND BEN-PORATH, M.: Elimination of Liver Interference from the Selenomethionine Pancreas Scan; *Journ. Nuclear Med.* **7**:387, 1966.

2. BLAU, M., MANCKE, R. F., AND BENDER, M. A.: Clinical Experience with Selenomethionine for Pancreas Visualization. *Journ. Nuclear Med.* **3**:202, 1962.

3. SODEE, D. B.: Radioisotope Scanning of the Pancreas with Selenomethionine (^{75}Se), *Radiology* **83**:910, 1964.

4. BLAU, M., Pancreas Scannings with Se^{75} Selenomethionine, Medical Radioisotope Scanning **2**:275 IAEA, Vienna, 1964.

5. SODEE, D.B.: Radioisotope Scanning of the Pancreas with Selenomethionine Se^{75}, Medical Radioisotope Scanning **2**:289 IAEA, Vienna, 1964.

6. HAYNIE, T. P., SVOBODA, K. C. AND ZUIDEMA, G. D.: Diagnosis of Pancreatic Disease by Photoscanning; *Journ. Nuc. Med.* **5**:90-94, 1964.

7. TABERN, D. L., KEARNEY, J. AND DOLBOW, A.: The Use of Intravenous Amino Acids in the Visualization of the Pancreas with Seleno 75 Methionine; *Journ. Nuclear Med.* **6**:762-766, 1965.

8. RODRIGUEZ, ANTUNEZ, A.: The Use of Morphine in Pancreatic Scanning with ^{75}Se Methionine. *Journ. Nuclear Med.* **5**:729, 1964.

9. BURDINE, J. A. AND HAYNIE, T. P.: Diagnosis of Pancreatic Carcinoma by Photoscanning; *Journ. AMA* 979-981, 1965.

10. ARONOW, S., THORS, R. AND G. L. BROWNELL: Positron Scanning of Liver and Pancreas, Medical Radioisotope Scanning 105, *IAEA*, Vienna, 1959.

_____ BENDER, M. A.: *ibid* 123.

11. SCHEPERS, H. AND WINKLER, C.: An Automatic Scanning System Using A Tape Perforator and Computer Technique, Medical Radioisotope Scanning **1**:321 IAEA, Vienna, 1964.

12. SPENCER, R. P.. Simultaneous Use of Two Radioisotopes by Scanner Plus Analogue Computer Coupling, *Journ. Nuclear Med.* **6**:844, 1965.

13. BEN-PORATH, M., CLAYTON, G. AND KAPLAN, E.: Selective Visualization of the Pancreas my a Subtractive Double Radioisotope Scanning Technique. Trans. of the American Nuclear Soc. 9 (In Press) 1966.

14. BUTSCH, W. C., MCGOWAN, J. M., AND WALTERS, W. W.: Clinical Studies on the Influence of Certain Drugs in Relation to Biliary Pain and to the Variations in Intrabiliary Pressure. *Surg. Gynec. & Obst.* **63**:451-456, 1936.

15. THOMAS, J. E.: Mechanism of Action of Pancreatic Stimuli Studied by Means of Atropine-like Drugs. *Am. J. Physiol.* **206**:124-128, 1964.

16. SANGSTER, A. J.: The Uses of Morphine and Propantheline in Intravenous Cholecystography. *Lancet.* **2**:525-527, 1955.

17. OLDENDORF, W. H. AND KITANO, M.: Selenomethionine Reappearance in Blood Following Intravenous Injection, *Journ. Nuc. Med.* **4**:231, 1963.